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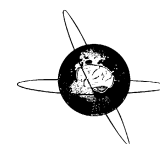
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Error and feedback processing in children with ADHD and children with Autistic Spectrum Disorder: An EEG event-related potential study

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ABSTRACT

Objective: Performance monitoring was investigated in typically developing (TD) children, children with Autistic Spectrum Disorder (ASD), and Methylphenidate (Mph)-treated and medication-free children with Attention Deficit Hyperactivity Disorder (ADHD).

Methods: Subjects performed a feedback-based learning task. Event-related Potentials (ERPs) time locked to responses and feedback were derived from the EEG.

Results: Compared to the TD and ASD groups, the medication-free ADHD group showed a decreased response-locked Error Related Negativity (ERN) and error Positivity (Pe), particularly as learning progressed throughout the task. Compared to the medication-free ADHD group, the Methylphenidate-treated group showed a normalised Pe. All clinical groups showed or tended to show a decreased feedback-locked late positive potential to negative feedback.

Conclusions: The ERPs suggest that medication-free children with ADHD, but not with ASD, have a diminished capacity to monitor their error responses when they are learning by performance feedback. This capacity partially 'normalises' in Mph-treated children with ADHD. Both children with ADHD and children with ASD are suggested being compromised in affective feedback processing.

Significance: This study shows that measuring ERPs of error and feedback processing is a useful method for (1) dissociating ADHD from ASD and (2) elucidating medication effects in ADHD on component processes of performance monitoring.

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1. Introduction

1.1. Objective

Although Attention Deficit Hyperactivity Disorder (ADHD) and Autistic Spectrum Disorder (ASD) are described as clearly distinct syndromes in the DSM-IV-TR (American Psychiatric Association, 2000), in clinical practice it often appears difficult to discriminate between the two disorders (Clark et al., 1999; Jensen et al., 1997). Phenomenological studies report that many children with ADHD also have ASD symptoms and vice versa (see for a review: Nijmeijer et al., 2008) and there is an increasing body of research suggesting genetic overlap between the two disorders (Ronald et al., 2008; Smalley et al., 2005). Moreover, both ADHD and ASD have been related to executive functioning (EF) deficits (Geurts et al., 2004; Happé et al., 2006; Ozonoff and Jensen, 1999), although there is an ongoing discussion on the type of EF profile that is specific for each disorder. This study uses electrocortical

measures to investigate specific aspects of EF processes in children with ASD, Methylphenidate-treated and medication-free children with ADHD and a group of typically developing (TD) children. This approach may allow for discriminating children with ASD and ADHD on specific EF processes, as well as for investigating effects of the first-choice treatment of ADHD on these processes.

The EF ability targeted in this study concerns performance monitoring; the ability to continuously monitor whether action goals have been reached in order to optimise future behaviour (Stuss et al., 1995). This ability can be investigated by extracting event-related potentials (ERPs) from the electroencephalogram (EEG) that are time locked to responses and feedback stimuli, reflecting internal and external monitoring processes, respectively (Falkenstein et al., 1991; Gehring et al., 1990; Miltner et al., 1997; Müller et al., 2005). The children performed a probabilistic learning task, in which they were required to learn stimulus-response combinations by making use of performance feedback. An earlier study, which included the present group of TD children demonstrated that while learning progresses throughout the task, feedback-locked ERP-components (prefeedback Stimulus Preceding Negativity, P2a and P3) decrease, while the response-locked ERP-compo-

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nents (Error Related Negativity and error Positivity) increase. This reflects that during learning children become less dependent on feedback stimuli, while depending more and more on their internal monitoring system, i.e. they shift from an external mode of performance monitoring to an internal mode (Groen et al., 2007).

Although ERP research does not allow for direct interpretations in terms of deficient brain structures and neurotransmitter systems, indirect inferences can be made thanks to the large body of fundamental research on this topic. In the remainder of the Introduction a set of response and feedback monitoring components is described, that may be used for dissociating ADHD from ASD and for studying effects of Mph intake in children with ADHD.

1.2. Response monitoring in ADHD and ASD

The Error Related Negativity (ERN) is a negative-going waveform peaking just after an error response or negative feedback stimulus (Falkenstein et al., 1991; Gehring et al., 1990; Miltner et al., 1997). This component is thought to reflect a mismatch between actual and intended actions or goals and, therefore, occurs in response to unfavourable outcomes, response errors, response conflict and decision uncertainty (Ridderinkhof et al., 2004). Its neuronal source has been localised in the Anterior Cingulate Cortex (ACC) (see for a review: Taylor et al., 2007). The ERN is hypothesised to reflect phasic ACC activity in response to reinforcement signals from the mesencephalic dopamine system that serves as a trigger for further processing of the event and further deliberate compensatory behaviour (Holroyd and Coles, 2002). Further conscious error processing is thought to be reflected by the error Positivity (Pe), which is a positive-going potential following the ERN. Contrary to the ERN, this component does not emerge on trials where the subject is unaware of his committed error (Nieuwenhuis et al., 2001; O'Connell et al., 2007; Overbeek et al., 2005). Several studies have suggested that the Pe is a P3(b) response to the processing of errors (Davies et al., 2001; Leuthold and Sommer, 1999; O'Connell et al., 2007; Overbeek et al., 2005). A recent theoretical framework has proposed that the P3 reflects a phasic response of the locus coeruleus-noradreneline (LC-NE) system to the outcome of internal decision-making (Nieuwenhuis et al., 2005). Therefore, Overbeek and colleagues (2005) suggest that error awareness, as reflected by an enlarged Pe amplitude, is associated with increased phasic noradrenergic activity of the LC-NE system.

Findings on the ERN amplitude in ADHD are inconsistent. Two studies have found reduced ERN amplitudes in children with ADHD compared to TD children, suggesting that they have a deficit in monitoring ongoing behaviour (Liotti et al., 2005; Van Meel et al., 2007). Wiersma and colleagues (2005) as well as Jonkman and colleagues (2007), however, could not reveal differences in ERN amplitude between children with ADHD and TD children. Burgio-Murphy and colleagues (2007), finally, reported an enlarged ERN amplitude in children with ADHD (combined type) and suggest that they are more emotionally reactive. The Pe is fairly consistently found to be decreased in children with ADHD, suggesting that they become less aware of their committed errors (Jonkman et al., 2007; Overtoom et al., 2002; Wiersma et al., 2005; but see: Burgio-Murphy et al., 2007). Reduced Pe amplitudes in ADHD are in accordance with the findings of reduced post error compensatory behaviour, i.e. the strategic reaction time (RT) slowing after the commission of errors (Schachar et al., 2004; Sergeant and Van der Meere, 1988; Wiersma et al., 2005). Reduced error awareness may thus hamper children with ADHD in adequately adapting their behaviour and consequently in learning from their mistakes.

Methylphenidate (Mph) is a stimulant that is widely used for the treatment of ADHD symptoms, and is known to block the re-

uptake of both dopamine and noradrenaline, thereby enhancing their extracellular release (Pliszka, 2005; Seeman and Madras, 1998). Although sample sizes were small, a recent placebo-controlled study revealed that Mph improves error processing in children with ADHD (Jonkman et al., 2007). In this study children with ADHD treated with Mph showed a normalised error-related Pe amplitude. This finding is in line with some performance studies, showing that Mph increases post error slowing in children with AD(H)D (De Sonneville et al., 1994; Krusch et al., 1996). In contrast to studies showing that stimulants like Mph enhance response-locked ERN amplitudes in healthy adults (De Bruijn et al., 2004; De Bruijn et al., 2005), Jonkman and colleagues, however, did not find a modulating effect of Mph on the ERN in children with ADHD. This suggests that Mph improves conscious error processing but not error detection in ADHD.

Concerning ASD, several neuroimaging studies have found support for a hypofunctional ACC in autism (Gomot et al., 2006; Haznedar et al., 2000; Ohnishi et al., 2000), with two of them reporting that ACC activity is negatively associated with symptom presentation in autism (Haznedar et al., 2000; Ohnishi et al., 2000). There is also evidence that 'mentalising' tasks which are difficult for subjects with ASD, like joint attention and Theory of Mind tasks, recruit brain areas that are overlapping with brain areas involved in the generation of the ERN (Amodio and Frith, 2006; Frith and Frith, 2001; Mundy, 2003). Henderson and colleagues (2006) were the first and only authors to date who conducted an electrophysiological study on performance monitoring in children diagnosed with ASD. They could, however, not reveal overall differences in ERN amplitude between the ASD and TD groups, but found that within the ASD group larger ERN amplitudes were predictive of a smaller impairment in social interaction as well as of decreased internalising problems. The authors suggest that a response monitoring deficit may not be a core feature of ASD, but that a measure like the ERN might serve as 'a bio-behavioural marker of cognitive processes that moderate the development of children with autism' (p. 106, Henderson et al., 2006).

Performance studies have suggested deficits in error correction in autism. Russell and Jarrold (1998), for example, found that autistic children were more likely to fail correcting errors than controls, both when they were provided with visual feedback about their errors (external monitoring) and when they had to detect their errors themselves (internal monitoring). Bogte and colleagues (2007), moreover, found that a group of adult autistic subjects showed no post error slowing, whereas a control group did. These studies suggest decreased error awareness in autism, predicting decreased Pe amplitudes.

1.3. Feedback monitoring in ADHD and ASD

ERP research regarding feedback processing has predominantly focussed on the feedback ERN (Miltner et al., 1997; Müller et al., 2005). However, in our previous study, which included the same group of TD children performing the present learning task, we could not identify this component. Instead, a P2a, P3 and later occurring positivity were elicited, all of them being increased to negative opposed to positive feedback (Groen et al., 2007). A study examining feedback-related ERPs in children with ADHD (Van Meel et al., 2005) also described such early frontal positivity (but also a clear feedback ERN), which was enlarged in response to stimuli indicating loss. Compared to TD children, children with ADHD showed a reduced P2a amplitude to both positive and negative feedback stimuli, suggesting that the early discrimination or categorisation of motivationally relevant stimuli is compromised in these children (Van Meel et al., 2005). Additionally, children with ADHD showed a decreased late positivity (after 450 ms) to negative feedback stimuli indicating loss. This latter finding had

been interpreted as a deficit in the affective evaluation of feedback signals and altered evaluation of future consequences in children with ADHD (Van Meel et al., 2005).

Another study submitted by Van Meel and colleagues (in preparation) investigated the anticipation of feedback stimuli in children with ADHD. The authors observed a prefeedback Stimulus Preceding Negativity (SPN), a negative-going slow wave that has been associated with the anticipation of the affective motivational value of feedback stimuli (for an overview see: Böcker et al., 2001). Compared to TD children, children with ADHD showed decreased prefeedback SPN amplitudes (Van Meel et al., In preparation). This is in line with repeated findings of decreased amplitudes of a similar negative slow wave in anticipation of target stimuli in ADHD, the Contingent Negative Variation (see for a review: Barry et al., 2003). Diminished negative slow waves in anticipation of upcoming task-relevant information in ADHD may be interpreted as deficient preparatory control processes that are due to diminished motivational involvement in task situations (Sergeant and Van der Meere, 1988).

Regarding autism, there is no literature available on performance monitoring components other than the response-locked ERN. ERP research on autism has mainly focussed on perceptual and attentional processing and has generally yielded inconsistent findings because of methodological problems (see for a review: Kemner and Van Engeland, 2006). Several performance studies have, however, investigated the differential sensitivity to social versus non-social reward and feedback in autistic children. These studies all show that, compared to TD children, autistic children are less sensitive to social feedback, e.g. smiling or words of appreciation, while they show no deficient sensitivity to non-social feedback, e.g. money or sensory feedback (Dawson et al., 2002; Garretson et al., 1990; Ingersoll et al., 2003). Yet, other studies did suggest an impairment in sensitivity to non-social feedback (Althaus et al., 1996) and reward (Dawson et al., 2001). This study may contribute to the scarce literature on feedback sensitivity in ASD by measuring feedback related ERPs in age and intelligence matched groups of children.

1.4. Expectations

Both children with ADHD and children with ASD are hypothesised to both show smaller response and feedback related monitoring components than age and intelligence matched TD children. The inclusion of a group of children with ADHD who took their normal dose of Mph at the time of the experiment, moreover, allows for studying the effect of stimulant medication in children with ADHD on performance monitoring. In agreement with a recently published study by Jonkman and colleagues (2007), we expect that Mph selectively influences response monitoring components in children with ADHD, with a stimulating effect on especially the Pe. Concerning feedback monitoring, Mph-treated children with ADHD may also show larger components than the medication-free children with ADHD and may, therefore, be more similar to TD children.

2. Methods

2.1. Subjects

The study included 72 10- to-12-year-old children who belonged to four experimental groups: a typically developing (TD) group ($n = 18$), a medication-free ADHD group ($n = 18$), a Methylphenidate (Mph)-treated ADHD group ($n = 17$) and an ASD group ($n = 19$). The TD children were recruited from primary schools in the city of Groningen and by advertisement in the newsletter of

the University Medical Centre in Groningen (UMCG). The Child Behavioural Checklist (CBCL: Achenbach and Rescorla, 2001) was filled out by the parents of all children to assess a wide range of childhood psychopathology. None of the TD children scored within the clinical range of the total problem scale of this list, suggesting that they were free from clinical behaviour problems. The TD children, moreover, scored significantly lower on a parental questionnaire measuring social dysfunction: the Children's Social Behaviour Questionnaire (CSBQ: Hartman et al., 2006). See Table 1 for a summary of all group characteristics.

ADHD and ASD had been diagnosed by independent well-trained child psychiatrists of our Department of Child- and Adolescent Psychiatry, according to the diagnostic criteria of the DSM-IV-TR (American Psychiatric Association, 2000). Regarding ADHD, only children with the combined type were included, which required pervasiveness (at home and at school) of both inattentive symptoms and hyperactive-impulsive symptoms observed during at least 6 months. Some of the symptoms caused impairment before 7 years of age. Regarding the ASD group, the children showed serious and pervasive disabilities in the development of social and communicative skills, and presence of stereotype interests and behaviour. These symptoms, however, did not meet the criteria for a full-blown Autistic or Asperger Disorder because of late age onset, atypical symptomatology, or subthreshold symptomatology, or all of these, and were consequently diagnosed as having Pervasive Developmental Disorder Not Otherwise Specified (PDDNOS). After the diagnosis, ADHD and ASD symptoms were additionally assessed by standardised questionnaires (see below).

Written informed consent was obtained from all parents and all 12-year-old children assented to the study. The study was approved by the Medical Ethical Committee of the University Medical Center, Groningen.

Of the 35 children with ADHD, 31 children were Mph responders, who all took this drug during the main part of the year preceding the experiment. These Mph responders were randomly assigned to an Mph-treated or medication-free condition. Those assigned to the medication-free condition were asked to discontinue Mph-intake for at least 17 h before they entered the experiment. This period was considered long enough due to an expected clearance within 4–5 times the half-life of Mph, which is about 3.5 h. The remaining four of the 35 children with ADHD did not yet use medication and were, therefore, directly assigned to the medication-free group. All children in the ASD group were medication-free at the time of the experiment.

Table 1 shows a summary of the group characteristics and the corresponding post hoc comparisons. Intelligence was measured by assessing the Wechsler Intelligence Scale for Children-III (WISC-III) on another day than on the day of the experiment and all children had a full-scale Intelligence Quotient at or above 80. The four groups neither differed in age nor in intelligence (see Table 1). The ratio of boys and girls was approximately 5:1, which did not differ significantly between groups. As measured by a self-report list for handedness (Van Strien, 2003), the majority of the children was right handed or had a tendency to right handedness. The ratio of left: ambidexter: right did not differ significantly between groups.

For measuring ADHD symptoms in the clinical groups, the ADHD section of the Diagnostic Interview Schedule for Children-IV was administered to the parents (DISC-IV: Shaffer et al., 2000). The Dutch translation of this structured interview was used (Ferdinand and Van der Ende, 1998). Moreover, the Conners' Teacher Rating Scale- Revised (CTRS-R) was administered to the teachers of the clinical children (Conners, 1990; Conners, 1999). All children with ADHD scored either in the clinical range of the DISC-IV or in the borderline range of the CTRS-R. Except for five children, all children with ADHD scored within the clinical range of at least one of

Table 1
Group characteristics

Measures	TD n = 18 Ratio		ASD n = 19 Ratio		ADHD Mph n = 17 Ratio		ADHD n = 18 Ratio		chi square	Bonferroni corrected post hoc analyses
Handedness (left/ambidexter/right)	0/4/14		1/3/15		1/3/13		1/1/16		.81	–
Gender (male/female)	12/6		15/4		16/1		16/2		.16	–
Mph intake in past year (on/off)	0/18		1/18		17/0		14/4		<.001	TD,ASD*** < ADHD < ADHD Mph*
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p value	
Age (years)	11.4	0.9	11.4	0.9	11.4	0.8	11.6	0.8	.88	–
Total IQ	103	9.5	102	10.2	99	11.3	100	13.0	.61	–
Verbal IQ	107	10.4	102	12.3	99	12.7	102	10.4	.29	–
Performal IQ	97	12.8	102	11.1	98	12.3	97	16.4	.61	–
<i>Social Communication Questionnaire (SCQ)</i>										
Total	–		20.5	4.2	7.2	3.9	5.0	3.1	<.001	ADHD Mph, ADHD < ASD***
Social interaction	–		8.6	2.8	3.0	2.1	0.9	1.3	<.001	ADHD < ADHD Mph*; ADHD, ADHD Mph < ASD***
Communication	–		6.4	1.9	2.7	1.5	2.5	1.4	<.001	ADHD Mph, ADHD < ASD***
Repetitive and stereotype behaviour	–		4.2	1.5	1.0	1.0	1.4	1.3	<.001	ADHD Mph, ADHD < ASD***
<i>Children's Social Behaviour Questionnaire (CSBQ)</i>										
Total	7.2	7.8	47.7	13.6	31.6	14.0	28.8	9.9	<.001	TD*** < ADHD Mph, ADHD < ASD**
<i>Diagnostic Interview Schedule for Children (DISC) ADHD section</i>										
Attentional problems	–		7.1	5.0	11.6	4.6	14.0	3.6	<.001	ASD** < ADHD Mph, ADHD
Hyperactive impulsive behaviour	–		3.1	3.5	12.0	4.0	13.8	4.3	.000	ASD*** < ADHD Mph, ADHD
<i>Conners Teacher Rating Scale- Revised (CTRS-R)</i>										
Oppositional	–		50.4	7.8	60.6	11.3	58.5	13.4	<.05	ASD* < ADHD Mph
Inattentive/cognitive problems	–		52.7	11.0	53.0	6.5	58.3	13.7	.24	
Hyperactivity–impulsivity	–		53.2	6.3	64.4	10.7	64.9	14.3	<.01	ASD* < ADHD Mph; ASD** < ADHD
Anxious/shy	–		68.1	13.2	59.8	11.3	67.5	13.1	.10	
Perfectionism	–		55.6	11.8	54.6	12.6	54.2	8.9	.93	
Social problems	–		70.0	14.9	57.0	8.5	60.8	14.6	<.05	ASD* > ADHD Mph
ADHD index	–		55.3	10.7	60.8	8.5	64.6	15.0	.06	ASD < ADHD
<i>Child Behavioural Checklist (CBCL)</i>										
Total problems	14.8	11.5	52.6	23.3	50.2	27.9	59.6	20.0	<.001	TD*** < ADHD Mph, ADHD, ASD
Ratio: clinical/not clinical	0/18		10/9		7/10		11/7			
Internalizing problems	4.3	4.4	15.1	8.5	8.9	8.7	11.4	8.0	<.01	TD* < ADHD, ASD
Ratio: clinical/nsot clinical	1/18		11/8		3/14		8/10			
Externalizing problems	3.5	3.5	11.0	10.6	15.9	8.9	16.9	7.2	<.001	TD** < ADHD Mph, ADHD, ASD
Ratio: clinical/not clinical	0/18		5/14		8/9		8/10			

* p < .05.

** p < .01.

*** p < .001.

the ADHD subscales of the DISC-IV (attentional problems or hyperactive-impulsive problems). As 31 of the 35 children with ADHD were responding well to Mph, medication intake during the period that was questioned in the interview very likely caused lower scores than would have been obtained at the time of the diagnosis. This may explain why five children scored below threshold on both subscales of the DISC-IV ADHD section. These children were all Mph-responders, but still scored minimally four out of nine symptoms of at least one of the DISC-IV subscales. Most important, however, children in both ADHD groups showed significantly more attentional problems and hyperactive-impulsive behaviour than the children in the ASD group on the DISC-IV (see Table 1).

For assessing autistic-type behaviour in the clinical groups, parents were administered the Dutch translation of the Social Communication Questionnaire (SCQ; Rutter et al., 2004), which is a recently developed screening tool for ASD based on the Autism Diagnostic Interview-Revised (Lord et al., 1994). To date, two validation studies have revealed that the SCQ is a valid measure for discriminating ASD from non-ASD cases with a cut-off of ≥ 15 (Berument et al., 1999; Chandler et al., 2007). All children included in the ASD group scored at or above this cut-off. Additional information on the children's social functioning was derived from the CSBQ. The total scores of both questionnaires confirmed that the children with ASD showed significantly more autistic-like symptoms than the children with ADHD (see Table 1).

2.2. Task

2.2.1. Feedback conditions and stimulus material

All children were tested in the morning or the afternoon by means of a probabilistic learning paradigm originating from Holroyd and Coles (2002), which had been adopted in a curtailed form from Crone and colleagues (2004). In this learning task, four coloured pictures (A, B, C and D) belonging to the categories 'animals', 'fruits', 'music' and 'sports' (Microsoft Clipart®) were randomly presented to the children. For each of the four pictures, the children had to find out which of the two keys to press by attending the performance feedback after their response. The children were, however, ignorant of the two feedback conditions that were assigned to the stimuli. The first two stimuli (A and B) were followed by informative feedback. Pressing the left key to picture A resulted in positive feedback, whereas pressing the right key resulted in negative feedback. For picture B this coupling was opposite: pressing the left key to picture B resulted in negative feedback, while pressing the right resulted in positive feedback. The second two stimuli (C and D) were followed by uninformative feedback. The feedback valence for picture C was always positive and the valence for picture D was always negative; the feedback outcome, therefore, was independent of the child's response. The children randomly received nine learning blocks, each consisting of 96 stimulus presentations (trials). Each block initiated a new learning process, because each block contained four new pictures for which the correct stimulus-response combination had to be learned. In Table 2 the distribution of the feedback conditions within one task block is given. Note that by randomly presenting the pictures, the feedback conditions were randomly distributed within one block too. The number of trials for each feedback valence within the informative feedback condition was variable, because it depended on the error rate of the child. In the uninformative condition, the number of trials for both positive and negative feedback was 24. The total number of experimental trials was 864 (9*96).

Each trial started with the presentation of one of the four stimuli, which stayed on the screen for the total duration of the individual deadline time (thus not terminated by the response, see Section 2.2.2). The feedback stimulus appeared 1000 ms after stimulus offset and stayed on the screen for 1500 ms. The trial was closed by a

Table 2

Distribution of feedback conditions within one task block

Informational value	Picture	Valence	# Trials
<i>Task block consisting of 96 trials</i>			
Informative (48 trials)	A	Positive = left key	24 – error rate
		Negative = right key	error rate
	B	Positive = right key	24 – error rate
		Negative = left key	error rate
Uninformative (48 trials)	C	Positive = left and right key	24
	D	Negative = left and right key	24

Four pictures that were repeatedly presented in every task block were either coupled to informative feedback (A and B) or to uninformative feedback (C and D). Originally published in Groen et al. (2007).

variable Intertrial Interval (ITI), which lasted for 500, 750 or 1000 ms. See for a schematic overview of the trial structure Fig. 1.

2.2.2. Task instructions and procedure

In every block, the children were instructed to win as many points as they could. In order to elicit enough error trials for computing error-related potentials in the informative feedback condition, the children were, however, forced to respond quickly by instructing them also to respond within a response deadline. To take into account individual differences in response speed an individual deadline was computed for every child. This individual deadline time (mean reaction time + 10%) had been determined after practicing before the start of the experimental blocks in a special deadline determination block. When they responded too late a black square appeared on the screen, indicating a loss of two points. Positive feedback (green square) and negative feedback (red square) indicated the win or loss of one point, respectively. The children started with 52 points at the start of each task block, which could maximally add up to 100 points at the end of a block.

The children were seated on a comfortable chair in front of a computer screen in a room that was separated from a control room by a one-way screen. After a standardised instruction, the children performed a short practice block consisting of 24 trials, which was followed by the deadline block consisting of 96 trials. After application of the electrodes, the children performed the nine experimental blocks (each lasting between 6 and 7 min). After five experimental blocks there was a break of 20 min. At the end of the experiment the children received a present (a toy), independent of their scores.

2.3. Computation of performance measures

The probabilistic learning task was built and presented by means of the program E-Prime (version 1.1; Psychological Software Tools). Key type (left or right), reaction time (RT) and accuracy of the response were recorded for every trial. To investigate the process of learning each block was cut into four consecutive sections (quartiles), which were then averaged across the nine blocks. Three performance measures were computed for all quartiles: RTs, individual SDs of RTs and percentage of correct responses.

2.4. Electroencephalogram recordings and computation of ERPs

The EEG was recorded using a lycra stretch cap (Electro-Cap Center BV) with 21 electrodes, placed according to the 10-20 system (O1, Oz, O2, P3, P5, P7, Pz, P4, P6, P8, C3, Cz, C4, F3, Fz, F4, F7, F8, FP1, FPz and FP2). Vertical and horizontal eye movements were recorded with electrodes, respectively, above and next to the left eye. For all channels Ag-AgCl electrodes were used and impedances were kept below 10 k Ω . Using the REFA-40 system (TMS International B.V.), all channels were amplified with filters

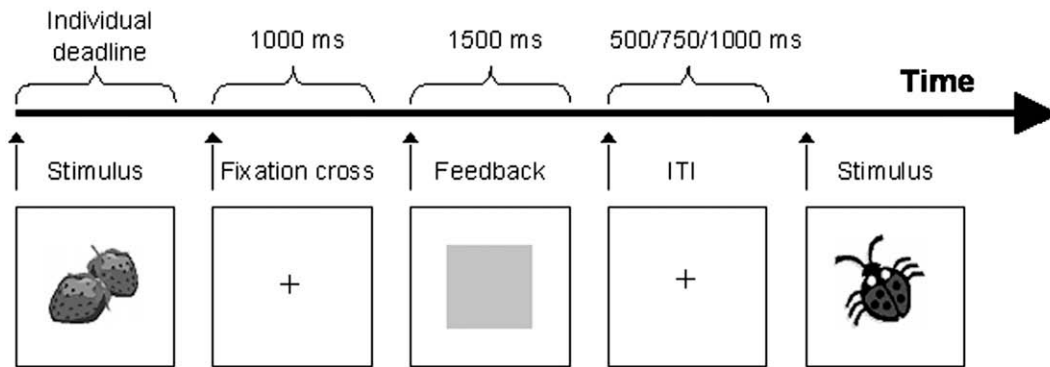


Fig. 1. Time course of a single trial. Within one task block each trial started with the presentation of one out of four stimuli. The feedback stimulus appeared 1000 ms after stimulus off-set and stayed on the screen for 1500 ms. The next trial started after a variable Inter Trial Interval (ITI) of 500, 750 or 1000 ms. Originally published in Groen et al. (2007).

set at a time constant of 1 s and a cut-off frequency of 130 Hz (low pass). The data from all channels were recorded with a sampling rate of 500 Hz using Portilab (version 1.10, TMS International B.V.). Using BrainVision (version 1.05, Brain Products), the signals were off-line filtered with a 0.25 Hz high pass and 30 Hz low pass filter, and referenced to the left ear electrode.

To investigate the ERN and Pe, EEG segments were cut around the children's responses ranging from 500 ms before to 800 ms after response onset, with the first 200 ms serving as a baseline. This was done for both response types, i.e. correct and incorrect responses. Segments for investigating prefeedback and feedback-induced ERPs were separately cut around the feedback stimulus, in order to keep the number of rejected segments due to artefacts as low as possible. For the prefeedback SPN, the segments ranged from 1000 ms before to 200 ms after feedback onset, with the first 200 ms of the segment serving as a baseline. For the feedback ERN and feedback P3, segments ranged from –200 ms to 1000 ms after feedback onset, with the first 200 ms serving as a baseline. All segments were scanned for artefacts. Segments with high or low activity (exceeding 200 μ V) and/or spikes and/or drift due to large eye-movements, head or body movements, or equipment failure were removed before the analyses. Segments with eye movements and blinks were kept and corrected, adopting the standard Gratton and Coles procedure (Gratton et al., 1983). For every child the segments were then averaged separately for all electrode positions and all feedback conditions. To investigate the process of learning each of the nine learning blocks was cut into two task sections (halves), which were then averaged across the nine blocks, i.e. for all first halves and second halves separately.

2.5. Data analyses

Performance measures were analysed by means of a repeated measures ANOVA (SPSS, version 14.0) with task section (quartile 1–4) as the within subject variable and group (TD, ASD, ADHD, ADHD Mph) as the between subjects variable. This was done for the mean percentage of correct responses, mean RT and individual SDs of RTs in the informative condition. Repeated contrasts for the factor quartile were computed to investigate changes from quartile to quartile.

For statistical analyses of the ERPs, mean amplitude values were computed for successive time intervals of the average of every ERP. This method allows for more precisely detecting latencies of effects than investigating one broad interval. For the relatively short-lasting components, i.e. ERN and P2a, 20 ms intervals were computed, while for relatively long lasting components, i.e. Pe, prefeedback SPN and later feedback-induced components, 50 ms intervals were

computed. For the response-locked ERPs, 20 ms mean amplitude values were computed in the time period of –300 to 100 ms for investigating the ERN, resulting in 20 intervals, and 50 ms mean amplitude values in the time period of 100–800 ms for investigating the Pe, resulting in 14 time intervals. For the feedback-induced ERPs, 20 ms mean amplitude values were computed in the time period of 120–240 ms for investigating the P2a, resulting in six intervals, and 50 ms mean amplitude values in the time period of 200–1000 ms for investigating later feedback-induced components, resulting in 16 intervals. The electrode positions of interest were Fz, Cz and Pz, as the ERN and feedback ERN have been described to have a midline frontocentral topography (Falkenstein et al., 1991; Gehring et al., 1993) and the Pe a more widespread centroparietal topography (Davies et al., 2001; Falkenstein et al., 1991). On all successive intervals repeated measures ANOVAs were conducted by applying a 3*2*2 design, with as within subject variables electrode position (Pz vs. Cz vs. Fz), response type (correct vs. incorrect) in case of response-locked segments or valence (positive vs. negative) in case of feedback-locked segments, and section (first vs. second section). The factor group (TD, ASD, ADHD, ADHD Mph) was used as the between subjects variable.

For the prefeedback ERPs, 50 ms mean amplitude values were computed in the time period of –800 to 0 ms, resulting in 16 intervals. The electrodes of interest for the prefeedback SPN were the left and right frontal, central and parietal electrode sites, because feedback manipulations have been shown to modulate this slow wave on these electrode positions (Chwilla and Brunia, 1991; Kotani et al., 2001). Repeated measures ANOVAs were conducted by applying a 3*2*2 design on each interval, with the within subject variables electrode position (F3/4 vs. C3/4 vs. P3/4), hemisphere (left vs. right), valence (positive vs. negative), and section (first vs. second section). Again the factor group (TD, ASD, ADHD, ADHD Mph) was used as the between subjects variable.

Main effects of group and interactions with group were specified for those intervals that were significant ($p < .05$) or showed a trend to significance ($p < .10$) with minimally medium effect sizes ($\eta^2 \geq .06$). Group differences were inspected by means of five post hoc pairwise group comparisons: TD vs. ASD, TD vs. ADHD Mph, TD vs. ADHD, ADHD vs. ADHD Mph, ADHD vs. ASD.

Because analyses were performed for multiple successive intervals there was an increasing risk of capitalisation on chance. Therefore, effects were only considered meaningful if three or more consecutive intervals were significant ($p < .05$) or showed a trend to significance ($p < .10$) in combination with a minimally medium effect size ($\eta^2 \geq .06$). The chance of finding three consecutive effects with each showing a significance level of at least $p = .10$ in a series of 20 intervals (e.g. in case of the ERN) is reduced to

$18 * 0.10 * 0.10 * 0.10 = 0.018$, which is below the significance criterion of $p = .05$. In case of the P2a, which is a rather short-lasting component investigated in only six intervals, two consecutive effects with $p < .10$ were considered to suffice, for the chance of finding two consecutive effects, each with $p = .10$, is $5 * 0.10 * 0.10 = 0.05$. From periods with ranges of (nearly) significant successive intervals, the minimum and maximum F -values (F_{\min} and F_{\max}) are reported with the smallest corresponding levels of significance. For all of the above-mentioned analyses, Greenhouse–Geisser adjusted p -values and the epsilon correction factor are reported for within subject factors with more than two levels, with the unadjusted degrees of freedom and F -values. Moreover, the partial eta squared effect sizes (η^2) are reported (Stevens, 2002).

3. Results

In the following section, only the informative feedback condition will be described, because this condition provides most information on performance monitoring processes. A previous report on the present sample of TD children indicated that in the uninformative condition less performance monitoring activity is present than in the informative condition, suggesting that the task manipulations were effective (Groen et al., 2007).

3.1. Performance measures

3.1.1. Accuracy

First of all, the groups neither differed in the duration of their individual deadlines (mean 785 ms, SD 93 ms) nor in their percentage of late responses (mean 6%, SD 5.5%). Trials with late responses were excluded from further analyses. As can be seen in Fig. 2, the overall accuracy on the probabilistic learning task in the informative condition was higher for the TD group in comparison to all clinical groups, despite similar deadlines of their response times. This is expressed by an effect of group ($F(3,68) = 3.1, p < .05, \eta^2 = .12$) and significant contrasts of all clinical groups with the TD group (TD vs. ADHD: $p < .01$; TD vs. ADHD Mph: $p < .05$; TD vs. ASD: $p < .05$). All groups increased in accuracy as the learning task progressed, but the learning rate, i.e. the steepness of the learning curves, did not differ between groups. This is expressed by a main effect of quartile ($F(3,204) = 202.2, p < .001, \eta^2 = .75$) and the absence of an interaction of quartile with group. In Fig. 2 this can be observed as an increase in accuracy across quartiles.

3.1.2. Reaction times

Within the informative condition the groups did not differ in their mean RT for correct trials, and none of the groups showed a learning effect for these RTs as the learning task progressed (see Fig. 2). All groups, however, showed a decrease in RT variability as the task progressed, which is expressed by a main effect of quartile for the individual SDs of RTs ($F(3,204) = 68.2, p < .001, \eta^2 = .50$) and absence of an interaction with group. In Fig. 2, this can be seen as a decrease in the magnitude of the individual SD of RTs across quartiles. Overall, however, the medication-free ADHD group was more variable in their correct RTs than the TD group (see Fig. 2). This is expressed by a main effect of group for the individual SDs of RTs ($F(3,68) = 3.3, p < .05, \eta^2 = .13$), (nearly) significant contrasts of all groups with the medication-free ADHD group (ADHD vs. TD: $p < .01$; ADHD vs. ADHD Mph: $p < .05$; ADHD vs. ASD: $p < .10$), and absence of significant contrasts among the other groups.

In the informative condition the children were faster on incorrect trials than on correct trials (463 ms vs. 496 ms), except for the medication-free ADHD group (481 ms vs. 487 ms). This is expressed by a significant effect of response type ($F(1,68) = 89.5$,

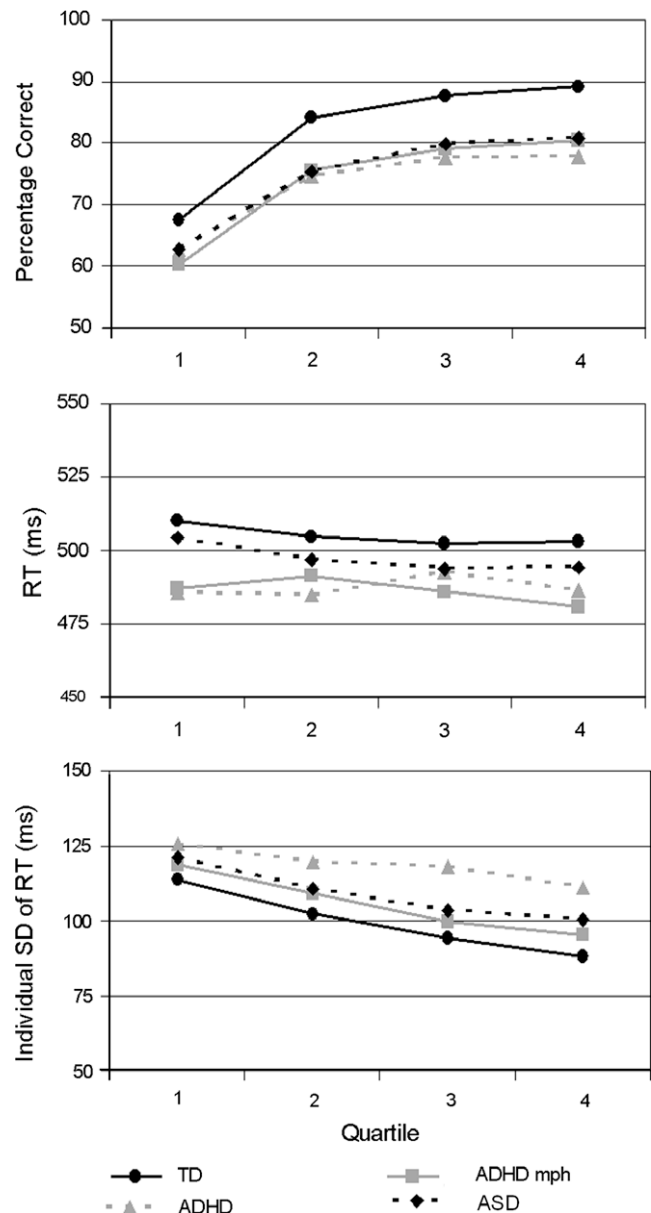


Fig. 2. Performance measures for four successive task sections. From top to bottom, the percentage of accurate responses, mean reaction time (RT) and individual standard deviations (SDs) of RTs in the informative condition are depicted.

$p < .001, \eta^2 = .57$) and an interaction of group by response type ($F(3,68) = 6.9, p < .001, \eta^2 = .23$), with significant contrasts indicating that the difference between incorrect and correct RTs was smaller in the medication-free ADHD group than in the other groups (ADHD vs. TD: $p < .001$; ADHD vs. ADHD Mph: $p < .01$; ADHD vs. ASD: $p < .01$). The other groups did not differ.

3.2. ERPs

Number of trials in the ERP analyses. When measuring EEG, it is more difficult in children than in adults to obtain ERPs that are free from artefacts resulting from head movements and eye movements (De Boer et al., 2005). This holds to an even greater extent for children suffering from ADHD. In some children not enough artefact-free error trials could be obtained in the second task half, due to low error rates in combination with high artefact frequencies. This explains the deviant degrees of freedom in some comparisons.

3.2.1. Response-locked potentials

3.2.1.1. ERN (–300 ms to 100 ms). Within the ERN period an overall effect of response type was present at Fz from –120 to 80 ms ($F_{\min}(1,66) = 10.3$, $p < .01$, $\eta^2 = .14$; $F_{\max}(1,66) = 70.7$, $p < .001$, $\eta^2 = .52$) and at Cz from –180 to 80 ms ($F_{\min}(1,66) = 6.9$, $p < .05$, $\eta^2 = .10$; $F_{\max}(1,66) = 113.7$, $p < .001$, $\eta^2 = .63$). The amplitude of the ERN differed between groups at Fz only. This is expressed by interactions of response type by group from –40 to 80 ms at Fz with medium to large effect size ($F_{\min}(3,66) = 2.5$, $p < .10$, $\eta^2 = .10$; $F_{\max}(3,66) = 3.8$, $p < .05$, $\eta^2 = .15$) and absence of such interactions at Cz. Post hoc pairwise group comparisons are summarised in Table 3. As can be seen in Fig. 3, both the Mph-treated and medication-free ADHD groups showed smaller ERN amplitudes than the TD group. The ASD group did not differ from the TD group in ERN amplitude, but could be differentiated from the medication-free ADHD group with medium to large effect size. In Fig. 4A the mean ERN amplitudes, separated for task section, are given for each group.

3.2.1.2. ERN and learning (–300 ms to 100 ms). The ERN amplitude at Fz differed between the first and second sections, which is reflected by an interactions between response type and section from –40 to 100 ms ($F_{\min}(1,66) = 4.6$, $p < .05$, $\eta^2 = .07$; $F_{\max}(1,66) = 19.7$, $p < .001$, $\eta^2 = .23$). However, this learning effect differed between groups, which is reflected by interactions of response type by section by group from –40 to 100 ms with medium to large effect sizes ($F_{\min}(3,66) = 2.5$, $p < .10$, $\eta^2 = .10$; $F_{\max}(3,66) = 4.1$, $p < .01$, $\eta^2 = .16$). Post hoc pairwise group comparisons are summarised in Table 3, showing that both the Mph-treated ADHD group and the ASD group differ from the TD group in their learning effect on the ERN. As can be seen in Fig. 3, the ERN amplitude is larger in the second than in the first section for the TD group, and it appears to be smaller in the clinical groups. Analyses on the individual group level revealed that both the ASD and medication-free ADHD groups show an increase in ERN amplitude with learning, but that these effects lasted shorter than in the TD group, while the Mph-treated ADHD group did not show a significant learning effect. There were interactions of response type by section in the

ASD group from 0 to 80 ms ($F_{\min}(1,19) = 4.4$, $p < .10$, $\eta^2 = .20$; $F_{\max}(1,19) = 10.8$, $p < .01$, $\eta^2 = .38$), in the medication-free ADHD group from 20 to 80 ms ($F_{\min}(1,16) = 4.4$, $p < .10$, $\eta^2 = .23$; $F_{\max}(1,16) = 6.7$, $p < .05$, $\eta^2 = .31$), in the TD group from –100 to 60 ms ($F_{\min}(1,17) = 6.5$, $p < .05$, $\eta^2 = .28$; $F_{\max}(1,17) = 14.4$, $p < .001$, $\eta^2 = .46$), and such interactions were absent in the Mph-treated ADHD group. In Fig. 4A the mean ERN amplitudes, separated for task section, are given for each group.

3.2.1.3. Pe (100–800 ms). Within the Pe period a main effect of response type was present at Pz ranging from 100 to 650 ms ($F_{\min}(1,66) = 14.0$, $p < .001$, $\eta^2 = .18$; $F_{\max}(1,66) = 370.5$, $p < .001$, $\eta^2 = .85$). Although the overall interactions of response type and group showed only a trend to significance, effect sizes in the interval of 150 to 400 ms were medium ($F_{\min}(3,66) = 1.8$, $p < .10$, $\eta^2 = .08$; $F_{\max}(3,66) = 2.6$, $p < .10$, $\eta^2 = .11$). Post hoc pairwise group comparisons for the Pe amplitude at Pz, as summarised in Table 3, confirmed the impression from Fig. 3 that the medication-free ADHD group showed a decreased Pe amplitude than the TD group. The Mph-treated ADHD group and ASD group did not differ significantly from the medication-free ADHD group (p -values $> .05$), but these group differences approached significance showing medium effect sizes. In Fig. 4B the mean Pe amplitudes, separated for task section, are given for each group.

3.2.1.4. Pe and learning (100–800 ms). The effect of response type differed between the first and second sections, which is reflected by significant interactions of response type and section at Pz ranging from 100 to 550 ms ($F_{\min}(1,66) = 8.7$, $p < .05$, $\eta^2 = .12$; $F_{\max}(1,66) = 60.9$, $p < .001$, $\eta^2 = .48$). As can be seen in Fig. 3, the Pe is larger in the second section than in the first section, but this learning effect is found substantially smaller and of later appearance for the medication-free ADHD group than for the other groups. This finding is expressed by overall significant response type by section by group interactions ranging from 150 to 250 ms ($F_{\min}(3,66) = 3.2$, $p < .05$, $\eta^2 = .12$; $F_{\max}(3,66) = 3.9$, $p < .001$, $\eta^2 = .13$). Post hoc pairwise group comparisons for the section by response type interaction, as summarised in Table 3,

Table 3
Post hoc pairwise group comparisons among the experimental groups for the response-locked ERP components

	Fz: ERN amplitude Response type*group						Fz: ERN learning effect Response type*section*group					
	Interval (ms)	df	F	p	η^2		Interval (ms)	df	F	p	η^2	
TD vs. ADHD	–100 to 20	Min	1.32	3.0	.09	.09		Min		ns		
		Max	1.32	4.4	<.05	.12		Max		ns		
TD vs. ADHD Mph	–60 to 60	Min	1.33	3.6	<.05	.10	–100 to 20	Min	1.33	4.1	.05	.11
		Max	1.33	7.1	<.05	.18		Max	1.33	7.1	<.05	.18
TD vs. ASD		Min		ns			–40 to 40	Min	1.35	3.2	.08	.08
		Max		ns				Max	1.35	6.1	<.05	.18
ADHD vs. ADHD Mph		Min		ns				Min		ns		
		Max		ns				Max		ns		
ADHD vs. ASD	–160 to 60	Min	1.33	2.6	.10	.07		Min		ns		
		Max	1.33	5.5	<.05	.14		Max		ns		
	Pz: Pe amplitude Response type*group						Pz: Pe learning effect Response type*section*group					
	Interval (ms)	df	F	p	η^2		Interval (ms)	df	F	p	η^2	
TD vs. ADHD	150–400	Min	1.32	5.9	<.05	.16	150–250	Min	1.32	4.7	<.05	.13
		Max	1.32	8.4	<.01	.21		Max	1.32	5.8	<.05	.15
TD vs. ADHD Mph		Min		ns				Min		ns		
		Max		ns				Max		ns		
TD vs. ASD		Min		ns				Min		ns		
		Max		ns				Max		ns		
ADHD vs. ADHD Mph		Min		ns			100–400	Min	1.31	3.6	.07	.11
		Max		ns				Max	1.31	9.3	<.01	.23
ADHD vs. ASD		Min		ns			150–250	Min	1.33	3.3	.08	.09
		Max		ns				Max	1.33	6.3	<.05	.16

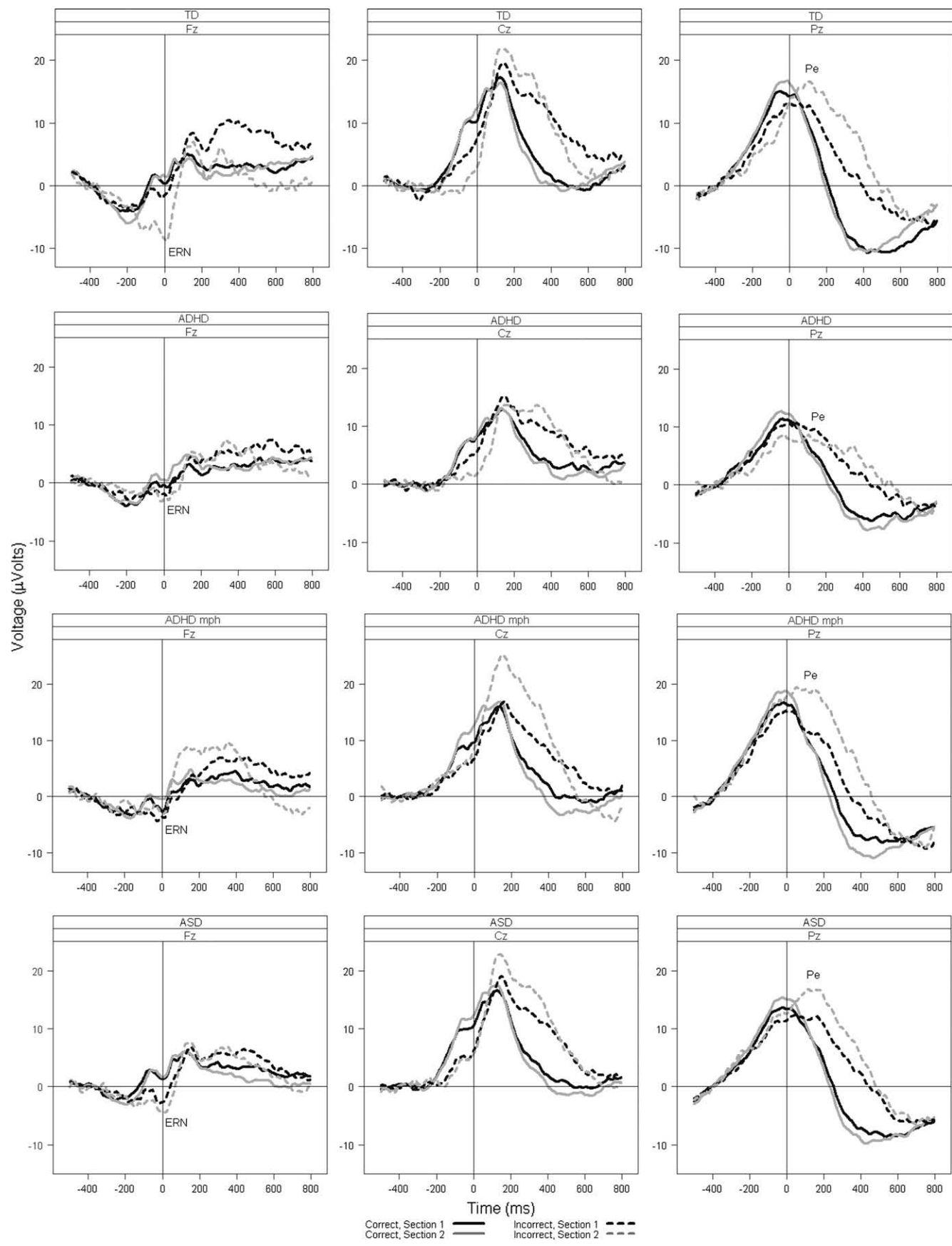


Fig. 3. Response-locked ERPs. ERP waveforms time locked to the response (0 ms) are depicted at Fz, Cz and Pz for the informative condition. For both the first and second sections of the task separate waveforms are shown for correct and incorrect responses.

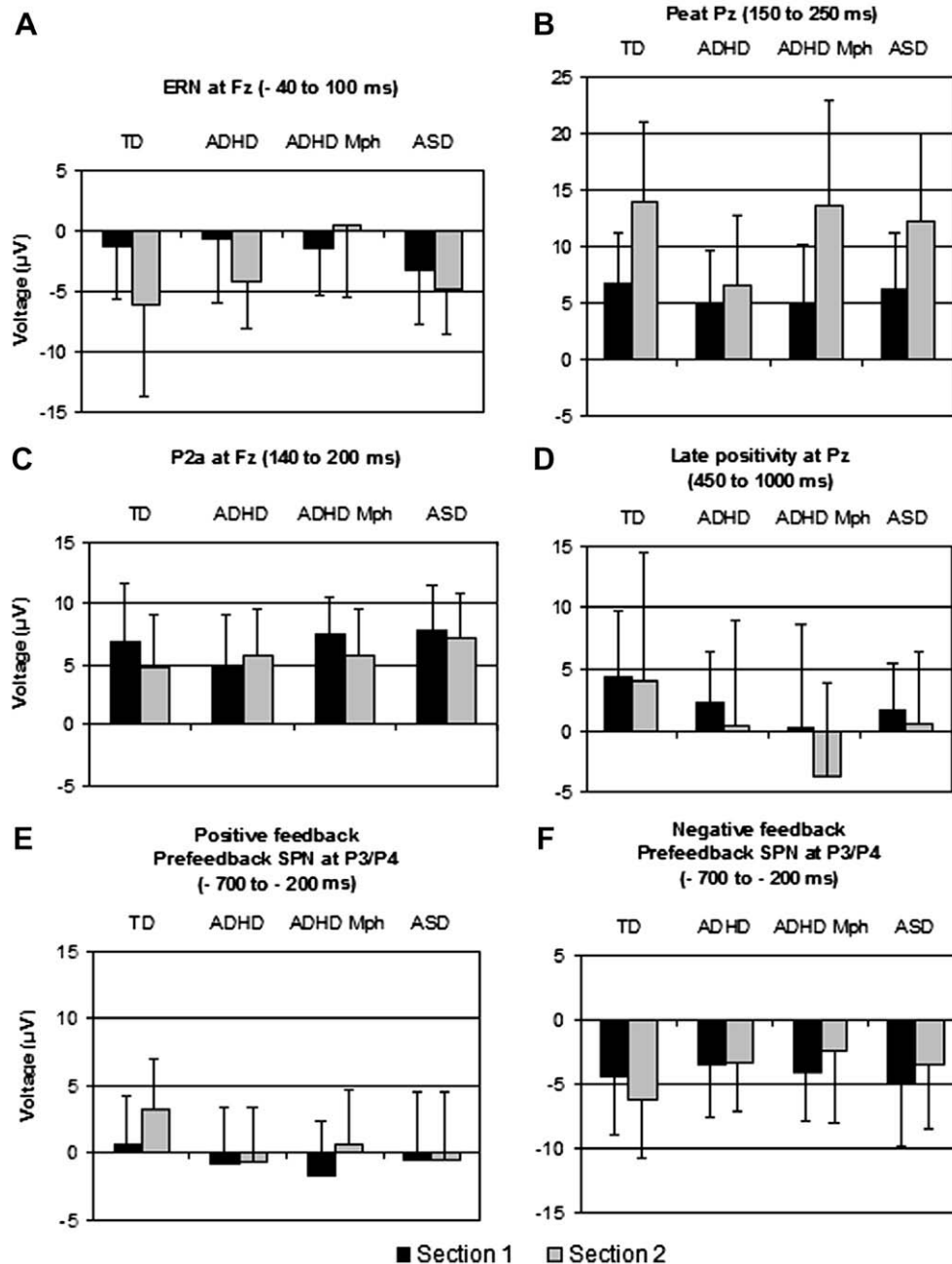


Fig. 4. Bar charts of mean ERP amplitudes. Mean amplitudes and standard deviations for the response- and feedback-locked ERPs are depicted for the first and second task sections separately. (A) and (B) Mean amplitude differences of incorrect minus correct responses of the ERN and Pe, respectively. (C) Mean absolute amplitudes of the P2a. (D) Mean amplitude differences of negative minus positive feedback of the late positivity. (E) and (F) Mean absolute amplitudes of the prefeedback SPN for positive and negative feedback, respectively.

revealed that the medication-free ADHD group differed significantly from the TD group. The medication-free ADHD group, moreover, differed (nearly) significantly from the ASD and Mph-treated ADHD group with medium to large effect sizes. In Fig. 4B the mean Pe amplitudes, separated for task section, are given for each group.

3.2.1.5. ERN/Pe and symptom presentation. For investigating possible associations between the ERN and Pe and the behavioural problems in the clinical groups, correlations were computed between the subscales of the SCQ as well as the DISC-IV ADHD section and difference values of these ERP components to correct incorrect responses. This was done separately for autistic symptoms (SCQ) in the ASD group and ADHD symptoms (DISC-IV) in the ADHD group.

Among the clinical groups, moreover, correlations were computed with the internalising and externalising scales of the CBCL.

The only nearly significant correlation found was a positive correlation between the CBCL internalising scale in the ERN amplitude at Fz ($r(52) = .26, p = .06$). This means that with increasing internalising problems, the ERN amplitude also increased. Inspection of the scatterplot indicated that neither outliers nor eventual subgroups of the internalising scale could explain this correlation.

3.2.2. Feedback-induced potentials

3.2.2.1. P2a (120–240 ms). As can be seen in Fig. 5, a positive peak can be observed at Fz and Cz around 185 ms after feedback onset. This frontal positive component has been described as the P2a or

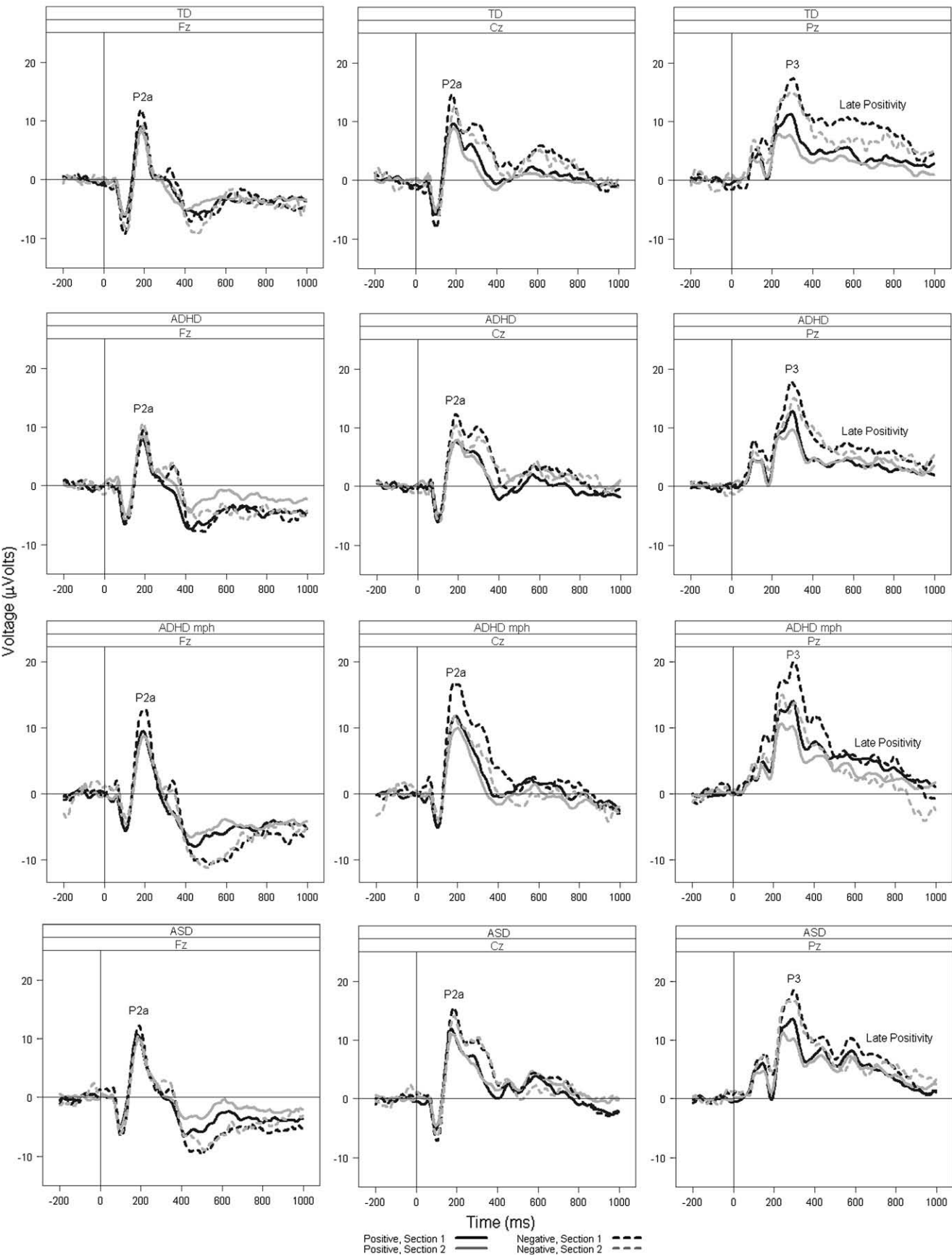


Fig. 5. Feedback-induced ERPs. Feedback-induced ERP waveforms time locked to feedback onset (0 ms) are depicted at Fz, Cz and Pz for the informative condition. For both the first and second sections of the task, separate waveforms are shown for positive and negative feedback.

Frontal Selection Positivity (Potts, 2004; Potts et al., 2006). The P2a was larger for negative feedback than for positive feedback, which is reflected by effects of feedback valence from 160 to 240 ms at Fz with small to large effect sizes ($F_{\min}(1,59) = 3.0$, $p < .10$, $\eta^2 = .05$; $F_{\max}(1,59) = 8.6$, $p < .01$, $\eta^2 = .13$) and large effect sizes at Cz ($F_{\min}(1,59) = 13.0$, $p < .001$, $\eta^2 = .18$; $F_{\max}(1,59) = 24.4$, $p < .001$, $\eta^2 = .30$). No group differences could be observed for this effect.

3.2.2.2. P2a and learning (120–240 ms). The P2a amplitude decreased from the first section of the task to the second section to an equal extent for positive and negative feedback. This is reflected by effects of section at Fz from 160 to 200 ms with small to medium effect sizes ($F_{\min}(1,59) = 3.1$, $p < .10$, $\eta^2 = .05$; $F_{\max}(1,59) = 5.0$, $p < .05$, $\eta^2 = .08$) and at Cz from 160 to 240 ms with medium to large effect sizes ($F_{\min}(1,59) = 4.4$, $p < .05$, $\eta^2 = .07$; $F_{\max}(1,59) = 17.5$, $p < .001$, $\eta^2 = .23$). Only at Fz did the groups differ in this effect from 160 to 200 ms, which is reflected by overall interactions of section by groups at Fz with medium effect sizes ($F_{\min}(1,59) = 2.3$, $p < .10$, $\eta^2 = .10$; $F_{\max}(1,59) = 2.8$, $p < .05$, $\eta^2 = .13$). Post hoc pairwise group comparisons, as summarised in Table 4, showed that the medication-free ADHD group differed from the TD, ASD and Mph-treated ADHD group in their effect of section. As can be seen in Fig. 5, all the latter groups showed a decrease in P2a amplitude from the first to the second sections, while the medication-free group did not. At Cz no group differences were present. In Fig. 4C the mean P2a amplitudes, separated for task section, are given for each group.

3.2.2.3. Feedback P3 and late positivity (200–1000 ms). For all groups, the P2a was followed by a positive component, which showed a centroparietal maximum and which was larger for negative than for positive feedback; the feedback P3. This is reflected by significant effects of feedback valence from 200 to 400 ms at Cz and from 200 to 500 ms at Pz (Cz: $F_{\min}(1,59) = 16.1$, $p < .001$, $\eta^2 = .21$; $F_{\max}(1,59) = 29.8$, $p < .001$, $\eta^2 = .34$; Pz: $F_{\min}(1,59) = 4.8$, $p < .05$, $\eta^2 = .08$; $F_{\max}(1,59) = 34.5$, $p < .001$, $\eta^2 = .37$). No group differences emerged in the early interval of the feedback P3, but after 450 ms the groups differed in their effect of valence for a late positivity (see Fig. 5). Although significant valence by group interactions at Pz was only short-lasting from 600 to 700 ms ($F_{\min}(3,59) = 2.5$, $p < .10$, $\eta^2 = .11$; $F_{\max}(3,59) = 3.0$, $p < .05$, $\eta^2 = .13$) and from 850 to 1000 ms ($F_{\min}(3,59) = 3.4$, $p < .05$, $\eta^2 = .15$; $F_{\max}(3,59) = 4.3$, $p < .01$, $\eta^2 = .18$), effect sizes of this interaction ranged from medium to large for all intervals between 450 and 1000 ms. Post hoc group comparisons, as summarised in Table 4, showed that the valence effects at Pz in for this late positivity were (nearly) significantly larger for the TD group than for the Mph-treated ADHD group and ASD group. This was, however,

not significant for the comparison of the medication-free children with ADHD and TD children, but effects for this comparison approached significance with small to medium effect size from 450 to 750 ms. In Fig. 4D the mean amplitude differences of the late positivity, separated for task section, are given for each group.

3.2.2.4. Feedback P3, late positivity and learning (200–1000 ms). Overall, the feedback P3 amplitude decreased from the first to the second sections at Cz and Pz independently of feedback valence, which can be seen in Fig. 5. At Cz this effect was confined to the feedback P3 interval from 200 to 350 ms (Cz: $F_{\min}(1,59) = 4.6$, $p < .05$, $\eta^2 = .07$; $F_{\max}(1,59) = 8.3$, $p < .01$, $\eta^2 = .12$), but at Pz this effect lasted to 750 ms after feedback onset (from 250 to 750 ms; $F_{\min}(1,59) = 6.6$, $p < .05$, $\eta^2 = .10$; $F_{\max}(1,59) = 20.7$, $p < .001$, $\eta^2 = .26$). There were no significant group differences for these learning effects.

3.2.3. Prefeedback potentials

3.2.3.1. Prefeedback SPN (–800 ms to 0 ms). In the interval between stimulus offset and feedback onset a negative slow wave developed in preparation of negative feedback for all groups (see Fig. 6). The prefeedback potential to positive feedback, however, was less negative than the potential to negative feedback for the clinical groups and, over centroparietal electrode positions, it was even positive for the TD group. Overall (for the electrode positions F3/F4, C3/C4, P3/P4), the prefeedback potentials were more negative over the right hemisphere than over the left, which is expressed by an effect of hemisphere from –400 to 0 ms ($F_{\min}(1,64) = 10.5$, $p < .05$, $\eta^2 = .14$; $F_{\max}(1,64) = 55.2$, $p < .001$, $\eta^2 = .46$). The effect of hemisphere was strongest over centrofrontal electrode positions, which is expressed by an overall interaction of electrode by hemisphere from –750 to 0 ms ($F_{\min}(2,128) = 6.1$, $p < .01$, $\eta^2 = .09$; $F_{\max}(2,128) = 19.3$, $p < .001$, $\eta^2 = .23$) and significant long-lasting effects of hemisphere with medium to large effect sizes at F3/F4 and C3/C4 (F3/F4 –500 to 0 ms: $F_{\min}(1,64) = 4.6$, $p < .05$, $\eta^2 = .07$; $F_{\max}(1,64) = 60.6$, $p < .001$, $\eta^2 = .49$; C3/C4 –500 to 0 ms: $F_{\min}(1,64) = 4.2$, $p < .05$, $\eta^2 = .06$; $F_{\max}(1,64) = 60.1$, $p < .001$, $\eta^2 = .48$). Yet, there were no significant interactions of hemisphere by group nor of hemisphere by valence and, therefore, this factor will not be taken into account in the further analyses.

Analyses at F3/F4, C3/C4 and P3/P4 revealed effects of feedback valence with a maximum at centroparietal electrode positions. This is reflected by significant interactions of electrode position by valence for the entire prefeedback period ($F_{\min}(2,128) = 4.6$, $p < .05$, $\eta^2 = .07$; $F_{\max}(2,128) = 9.9$, $p < .001$, $\eta^2 = .13$) with the effects being largest for parietal electrodes ($F_{\min}(1,64) = 18.2$, $p < .001$, $\eta^2 = .22$; $F_{\max}(1,64) = 57.4$, $p < .001$, $\eta^2 = .47$) and smaller for frontal electrode positions ($F_{\min}(1,64) = 5.9$, $p < .05$, $\eta^2 = .08$;

Table 4
Post hoc pairwise group comparisons among the experimental groups for the feedback-induced ERP components

	Fz: P2a learning effect Section*group						Pz: Late positivity amplitude Valence*group					
	Interval (ms)	df	F	p	η^2		Interval (ms)	df	F	p	η^2	
TD vs. ADHD	140–200	Min	1.29	3.6	.07	.11						
		Max	1.29	4.5	<.05	.14						
TD vs. ADHD Mph		Min			ns		450–950	1.29	3.4	.07	.11	
		Max			ns							
TD vs. ASD		Min			ns		500–700	1.33	3.6	.07	.10	
		Max			ns							
ADHD vs. ADHD Mph	140–220	Min	1.26	5.1	<.05	.16						
		Max	1.26	12.0	<.01	.32						
ADHD vs. ASD	160–200	Min	1.30	4.2	<.05	.12						
		Max	1.30	5.2	<.05	.15						

*Min' and 'Max' refer to the interval with the minimum *F*-value and maximum *F*-value, respectively, within the entire (nearly) significant period.

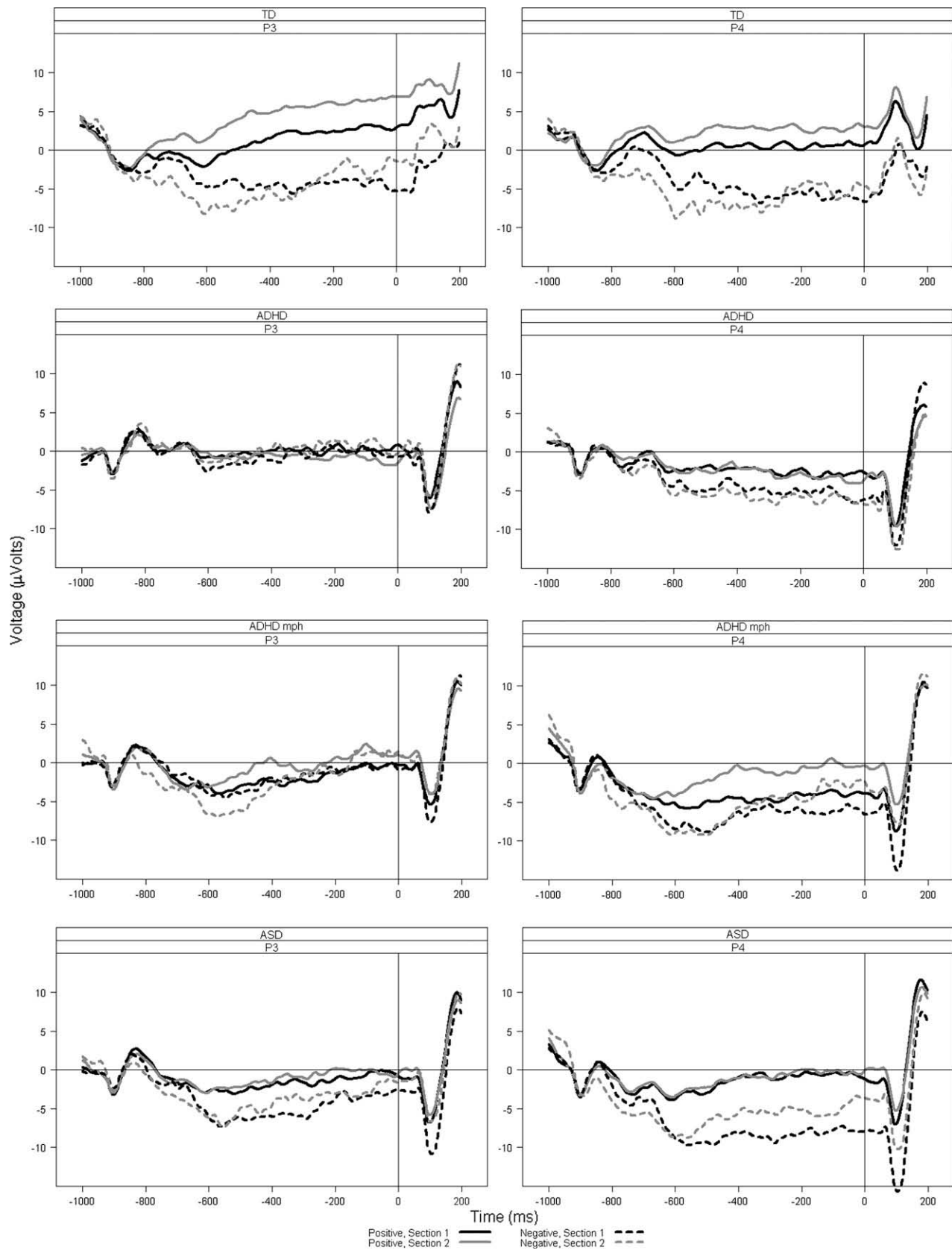


Fig. 6. Prefeedback ERPs. Prefeedback ERP waveforms time locked to feedback onset (0 ms) are depicted at P3 and P4 for the informative condition. For both the first and second sections of the task, separate waveforms are shown for positive and negative feedback.

$F_{\max}(1,64) = 39.3$, $p < .001$, $\eta^2 = .38$). As can be seen in Fig. 6, the clinical groups showed smaller differences between positive and

negative feedback than the TD group. These group differences were maximal at P3/P4 and, therefore, further analyses are confined to

Table 5

Post hoc pairwise group comparisons among the experimental groups for the prefeedback potentials

	P3/P4: Prefeedback potentials											
	Positive feedback: amplitude						Positive feedback: learning effect					
	Group						Section*group					
	Interval (ms)	df	F	p	η^2		Interval (ms)	df	F	p	η^2	
TD vs. ADHD	−500 to 0	Min	1.34	4.7	<.05	.12	−750 to 0	Min	1.34	2.2	ns	.06
		Max	1.34	9.9	<.01	.23		Max	1.34	11.5	<.01	.25
TD vs. ADHD Mph	−500 to 0	Min	1.33	4.0	.06	.11		Min			ns	
		Max	1.33	5.8	<.05	.15		Max			ns	
TD vs. ASD	−600 to 0	Min	1.35	2.6	ns	.07	−600 to 0	Min	1.35	3.3	.08	.08
		Max	1.35	4.2	<.05	.11		Max	1.35	6.7	<.05	.16
ADHD vs. ADHD Mph		Min			ns		−600 to 0	Min	1.33	1.8	ns	.05
		Max			ns			Max	1.33	4.5	<.05	.12
ADHD vs. ASD		Min			ns			Min			ns	
		Max			ns			Max			ns	
	Negative feedback: amplitude						Negative feedback: learning effect					
	Group						Section*group					
	Interval (ms)	df	F	p	η^2		Interval (ms)	df	F	p	η^2	
TD vs. ADHD		Min			ns			Min			ns	
		Max			ns			Max			ns	
TD vs. ADHD Mph		Min			ns		−750 to −350	Min	1.31	2.1	ns	.06
		Max			ns			Max	1.31	7.0	<.05	.19
TD vs. ASD		Min			ns		−700 to −250	Min	1.35	2.5	ns	.07
		Max			ns			Max	1.35	9.8	<.01	.22
ADHD vs. ADHD Mph		Min			ns		−550 to −350	Min	1.29	2.0	ns	.06
		Max			ns			Max	1.29	5.2	<.05	.15
ADHD vs. ASD		Min			ns		−550 to −250	Min	1.33	1.9	ns	.06
		Max			ns			Max	1.33	5.6	<.05	.15

'Min' and 'Max' refer to the interval with the minimum *F*-value and maximum *F*-value, respectively, within the entire (nearly) significant period.

this electrode pair. There was a significant valence by group interaction from –650 to 0 ms at P3/P4 ($F_{\min}(3,64) = 3.1$, $p < .05$, $\eta^2 = .13$; $F_{\max}(3,64) = 6.5$, $p < .01$, $\eta^2 = .23$) and no interaction with hemisphere. Further analyses were conducted for positive and negative feedback separately, because Fig. 6 suggested differential group effects for positive and negative feedback. The clinical groups showed similar prefeedback amplitudes to negative feedback as the TD group (see Table 5), whereas the prefeedback potential to positive feedback was more positive for the TD group than for all clinical groups (see Table 5). In Fig. 4E and F the mean prefeedback SPN amplitudes to positive and negative feedback, separated for task section, are given for each group.

3.2.3.2. Prefeedback SPN and learning (–800 ms to 0 ms). The groups differed in learning effects on their prefeedback potentials to positive and negative feedback. This is reflected by a significant valence by section by group interaction from –700 to –200 ms at P3/P4 ($F_{\min}(3,64) = 2.5$, $p < .10$, $\eta^2 = .11$; $F_{\max}(3,64) = 5.1$, $p < .01$, $\eta^2 = .19$). As can be seen in Fig. 6, in the TD and Mph-treated ADHD groups, the prefeedback potential to positive feedback grew more positive as the task progressed. The TD and Mph-treated ADHD groups differed (nearly) significantly from the medication-free ADHD group and ASD group for this learning effect, as reflected by post hoc pairwise group comparisons (see Table 5).

As can be seen in Fig. 6, the prefeedback potential to negative feedback of the TD group grew more negative as the task progressed, but this effect disappeared around 500 ms before feedback onset. The clinical groups did not show such early learning effect to negative feedback, as is reflected by post hoc pairwise comparisons with the TD group (see Table 5). Both the Mph-treated ADHD group and the ASD group showed a later learning effect; their prefeedback potential to negative feedback grew less negative with task progression from about 500 ms before feedback onset. From about –250 ms this learning effect for negative feedback, however, did no longer differ significantly from the TD group. The medication-free ADHD group did not show a learning effect for the prefeedback po-

tential to negative feedback, as is expressed by (nearly) significant post hoc pairwise comparisons with the Mph-treated ADHD group and the ASD group. In Fig. 4E and F the mean prefeedback SPN amplitudes to positive and negative feedback, separated for task section, are given for each group.

4. Discussion

4.1. Response monitoring

Recent psychophysiological and performance studies have suggested performance monitoring deficiencies in the developmental disorders ADHD and ASD. Although both children with ADHD and children with ASD performed worse on the probabilistic learning task than TD children, the ERP data in this study revealed a response monitoring deficit in children with ADHD only. This was reflected by decreased ERN and Pe amplitudes in medication-free children with ADHD compared to age and intelligence matched TD children and children with ASD. Apart from this, it must be mentioned that the ERN in this study showed a peak latency around response onset, which is much earlier than the usually observed peak latency between 40 and 100 ms in adults (Falkenstein et al., 1991; Gehring et al., 1990). The early peak latency may be explained by a time delay between electromyographic activity onset in the finger, to which the ERN may be closely time locked (Gehring et al., 1990), and the actual registered mechanical response. This time delay may be as long as 80 to 131 ms (Burle et al., 2002). However, the effects of response type emerged as early as 180 ms before the response, which has also been observed in previous developmental studies (although not explicitly mentioned in the text: Davies et al., 2004; Santesso et al., 2006). Such early error-related differences may, therefore, be specific for children and may deserve some more attention in future studies.

Notwithstanding the early occurrence of the ERN, the amplitudes of both the ERN and Pe suggest that children with ADHD have a deficit in both early error detection and later error aware-

ness. The finding of an attenuated ERN adds to the rather inconsistent literature on the size of the ERN amplitude in ADHD. One explanation for these inconsistent findings may be the heterogeneity of the investigated ADHD groups in general, with some patients having more attentional problems, others having more hyperactive-impulsive problems and still others showing comorbid problems like disruptive behaviour or internalising problems. As all these symptoms may be related to distinct neurobiological sources (Sagvolden et al., 2005), the outcomes of ERP research may be vulnerable to the composition of the samples, especially when samples are small. For future studies it is recommended to include larger samples of children with ADHD, allowing to control for differences in symptom presentation and comorbid conditions. A decreased response-related ERN in children with ADHD like in this study would, however, be in line with the bulk of neuroimaging studies suggesting that frontostriatal dopamine pathways are hypofunctional in ADHD (Bush et al., 2005; Castellanos and Tan-nock, 2002; Dickstein et al., 2006; Durston, 2003). A disturbance of frontostriatal processes, and a concomitant error processing deficit, may explain (part of the) self-regulatory problems that children with ADHD experience in everyday life, such as inconsistent, inaccurate and poorly regulated behaviour as well as deficits in self-regulated learning.

In contrast to the ERN, the finding of a smaller error-related Pe amplitude with increased learning in children with ADHD adds to a more consistent literature and thus strengthens the suggestion of reduced error awareness in ADHD. Reduced error awareness may hamper children with ADHD in learning from their mistakes and, on the longer term, to develop adaptive behaviour. As the Pe amplitude has been found to be related to post-error slowing in healthy adults (Hajcak et al., 2003; Nieuwenhuis et al., 2001), the attenuated Pe amplitude is in line with findings of reduced post error slowing in children with ADHD (Schachar et al., 2004; Sergeant and Van der Meere, 1988; Wiersema et al., 2005). Equivalent to the P3 (Nieuwenhuis et al., 2005), the Pe has been suggested to reflect phasic noradrenaline responses from the LC-NE system in response to errors (Davies et al., 2001; Leuthold and Sommer, 1999; O'Connell et al., 2007; Overbeek et al., 2005). In healthy brains, such quick arousal responses from the LC-NE system increase the state of alertness and sensory information processing (Berridge and Waterhouse, 2003). Decreased activity of this system, as reflected by an attenuated Pe amplitude, suggests that children with ADHD do not benefit as much from their errors as TD children do. An attenuated Pe in ADHD, moreover, agrees with the catecholamine hypothesis that next to the dopaminergic system, the NE system is involved in the pathology of ADHD (Pliszka, 2005).

Interestingly, children with ADHD that took their normal dose of Mph at the time of the experiment showed a normalised Pe amplitude, which is in agreement with the recent placebo-controlled study by Jonkman and colleagues (2007). Especially the learning effect on the Pe was larger for the Mph-treated ADHD group than for the medication-free ADHD group, while at the same time the Mph-treated ADHD group could not be differentiated from the TD group. Because of its hypothesised noradrenergic origin, the normalised Pe in Mph-treated children with ADHD may be explained by the stimulating effect of Mph on the noradrenaline system. Again agreeing with the study of Jonkman and colleagues (2007), Mph did not modulate the ERN amplitude in children with ADHD. This is contradictory to evidence from adult studies showing that stimulants like Mph boost the response-locked ERN amplitude (De Bruijn et al., 2004; De Bruijn et al., 2005). Concludingly, these data, as well as the data by Jonkman and colleagues, suggest that Mph improves conscious error processing in ADHD, but not early error detection. It may be hypothesised that the effect of Mph in children with ADHD, regarding performance monitoring

in particular, is mediated through its noradrenergic component rather than through its dopaminergic one.

In contrast to the ADHD group, the children with ASD showed no response monitoring deficits, as neither differences in overall ERN nor in Pe amplitude were found in comparison to TD children. This finding is in line with the only electrophysiological study on performance monitoring in ASD by Henderson and colleagues (2006), who also report an intact ERN in a similar ASD group. In contrast to the Henderson study, however, this study found no associations between response monitoring components and autistic-type symptoms within the ASD group. Although not specific to ASD, we did find that clinical children scoring high on internalising problems (i.e. withdrawn behaviour, somatic problems, anxious/depressive behaviour) show larger ERN amplitudes. This is in line with several adult studies showing that people characterized by high negative affect show increased ERN amplitudes (Hajcak et al., 2004). Apart from this relationship, spared internal monitoring in ASD contrasts with several performance studies suggesting self-monitoring deficits in ASD (Bogte et al., 2007; Mundy, 2003; Russell and Jarrold, 1998). It must be remarked, however, that these conclusions may not extend to patients suffering from the full-blown syndrome of autism or Asperger, because this study only included children with a sub-threshold form of autism.

4.2. Feedback monitoring

In none of the experimental groups did the feedback stimuli elicit a typical feedback ERN (for a detailed discussion on the possible causes of this remarkable finding, we refer to an earlier report; Groen et al., 2007). Instead, a frontocentral P2a component was observed, which has only recently been described to occur in response to feedback stimuli (Potts et al., 2006; Van Meel et al., 2005). In this study the P2a amplitude was larger for negative feedback than for positive feedback and may be interpreted as a general attentional reaction to motivationally salient stimuli, as this component has repeatedly been found to increase when the task relevance of stimuli increases (Falkenstein et al., 2003; Potts, 2004). Van Meel and colleagues (2005) also described a generally increased P2a in response to negative feedback, that, in contrast to our study, was found to be smaller in children with ADHD compared to TD children. The authors suggested that the early discrimination or categorisation of motivationally relevant stimuli may be disturbed in ADHD. This study could not replicate this finding and hence confirm such early disturbance of feedback processing in children with ADHD. The other way around, the medication-free children with ADHD did not show a decrease in P2a amplitude to negative feedback when learning the task. This suggests that for these children the negative feedback kept its relevance during the whole task, whereas it decreased in relevance with task progression for the other groups, i.e. the TD group, ASD group and the Mph-treated ADHD group.

Moreover, this study suggest deficits in late external feedback processing in both children with ADHD and children with ASD. The TD children showed an increased late positivity (from 450 ms after feedback onset) to negative opposed to positive feedback, which was attenuated in the ASD and Mph-treated ADHD groups. The comparison of the medication-free ADHD group and TD group did not reveal significant differences for this positivity, but in the investigated ERP period some group interactions approached significance and showed medium effect sizes. The direction of these non-significant effects is in agreement with the study by Van Meel and colleagues (2005), who also reported an attenuated late positivity to negative feedback in children with ADHD. We hypothesise that the observed late positivity is similar to the Late Positive Potential (LPP). The LPP is elicited by highly arousing

pleasant and unpleasant pictures and is thought to reflect increased attention to affective-motivational stimuli (Cuthbert et al., 2000; Hajcak et al., 2006; Schupp et al., 2000) and may, therefore, be the affective counterpart of the traditional P3. The LPP has been hypothesised to index perceptual processing in the visual cortex that is facilitated or amplified by amygdala-activity (Bradley et al., 2003; Hajcak et al., 2006). Decreased LPP amplitudes in children with ADHD and ASD may reflect diminished processing of negative feedback stimuli as a result of lower affective responsiveness to these stimuli. The clinical children in this study may not benefit from the affective value of negative feedback like the TD children do, i.e. they may suffer from decreased 'motivated attention' (Vuilleumier, 2005).

Different from the LPP, the 'traditional' P3 amplitude to the feedback stimuli (which in this study ranges from 200 to 450 ms after feedback onset) did not discriminate the children with ADHD and children with ASD from the TD children. All groups showed an enlarged feedback P3 to negative feedback compared to positive feedback, which may be the reflection of updating task-rules from long-term memory in response to error feedback (Donchin and Coles, 1988). Our finding of an intact feedback-related P3 in medication-free children with ADHD as well as a decreased response-related Pe appears contradictory to recent studies, proposing that both components have a similar neurobiological source (see for an overview: Overbeek et al., 2005). Further research should investigate the functional and neurobiological relationship of the response-locked Pe and feedback-locked P3.

4.3. Feedback anticipation

To complete our search for performance monitoring deficits in children with ADHD and in children with ASD we also investigated anticipatory processes before feedback onset by investigating prefeedback potentials. Different from our previous report (Groen et al., 2007), analyses of the prefeedback SPN in this study were extended to the entire prefeedback interval, because group differences appeared earlier than in the originally chosen interval just before feedback onset. Overall, the prefeedback SPN amplitude to negative feedback did not differ between groups, suggesting that the clinical groups have no fundamental problems in anticipating negative feedback. This finding in medication-free children with ADHD contrasts with the study by Van Meel and colleagues (in preparation), who found diminished prefeedback SPN amplitudes to negative feedback in their sample. In contrast to the TD children, the medication-free children with ADHD in this study did not show a decrease in prefeedback SPN amplitude with task progression, suggesting that they did not learn to predict the negative feedback, and that the negative feedback kept its relevance during the whole task. This finding is in accordance with the diminished learning effects on both the response-locked Pe and the feedback-locked P2a in this group. It may be speculated that the diminished Pe reflects why the negative feedback remains relevant to them: diminished conscious error processing at the time of the response makes it harder to predict the feedback outcome. This reasoning is also compatible with the findings in the Mph-treated children with ADHD; together with the 'normalised' Pe amplitude, they also showed 'normalised' learning effects on the P2a and prefeedback SPN. The ability of the Mph-treated children with ADHD to predict negative feedback and adjust anticipation may be related to the 'normalising' effect of Mph on the Pe amplitude.

Regarding the prefeedback potential to positive feedback, all clinical groups showed less positive, and even negative, prefeedback SPN amplitudes than the TD children. As a more negative amplitude of this potential has been related to increased anticipation of upcoming feedback stimuli (Bastiaansen et al., 2002; Böcker et al., 2001), a negative prefeedback SPN in the clinical groups, op-

posed to the positive potential in the TD group, suggests that upcoming positive feedback is more relevant to the clinical than to the TD children. One explanation may be that anticipation to positive feedback is less necessary for the TD children, because they are more confident about pressing the correct key. This is in correspondence with their higher level of accuracy on the task in comparison to the clinical groups. When considering the effects of task progression, the fact that only the TD and Mph-treated ADHD groups showed a more positive prefeedback potential, suggests that for these groups the upcoming positive feedback became less relevant as the task had been learned. The medication-free ADHD group and the ASD group did not show this learning effect, suggesting that for these groups positive feedback kept its relevance during the whole task.

In conclusion, the findings on the prefeedback SPN suggest that both children with ADHD and children with ASD do anticipate upcoming positive and negative feedback. In case of positive feedback, the medication-free ADHD group and ASD group may even attach more value to the upcoming feedback than the TD children, particularly as learning progresses throughout the task. The absence of learning effects on the prefeedback SPN to both positive and negative feedback in the medication-free ADHD group fits with the decreased learning effects on the response-locked and feedback-induced ERPs. We are rather reserved to draw conclusions about the underlying neurobiological origins of the prefeedback SPN in this study, because especially in the TD group, the appearance of this slow wave deviates from what has been described in adult literature, i.e. the timing of the effects and its polarity.

4.4. Conclusions

Both the Mph-treated and medication-free ADHD groups as well as the ASD group achieved a lower accuracy level than the TD group on the probabilistic learning task. The ERPs, however, revealed that the three groups could be differentiated on a set of component processes of error and feedback processing. In contrast to the TD children and children with ASD, the medication-free children with ADHD are suggested having a deficit in shifting from feedback monitoring to response monitoring while learning by performance feedback. This is reflected by decreased response monitoring components (ERN and Pe) and diminished learning effects on the feedback-related components (prefeedback SPN, P2a). Increased effects of learning on the ERPs in the Mph-treated ADHD group compared to the medication-free ADHD group provide some evidence for a modulating effect of Mph on response monitoring (Pe), feedback anticipation (prefeedback SPN) and feedback processing (P2a) in children with ADHD. The ASD group showed no deficits in response monitoring (ERN and Pe) and no deviating learning effects on negative feedback anticipation (prefeedback SPN) and early feedback processing (P2a). However, the ASD group as well as the Mph-treated ADHD group showed aberrant late feedback processing (LPP), suggesting diminished affective processing of external error information, i.e. 'motivated attention' in both disorders. Although the ERP figures and analyses also suggested such deficit in medication-free ADHD children, these effects did not reach statistical significance. Overall, this study shows that error and feedback-related ERPs are a useful tool for (1) dissociating ADHD from ASD and (2) elucidating medication effects in ADHD on specific aspects of EFs.

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